PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Form PCT/IPEA/416
C2673-PCT		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2004/001209	16.01.2004	16.01.2003

International Patent Classification (IPC) or national classification and IPC
A61K38/02, A61K39/00, C12N15/11, A61P7/00

Applicant
D. COLLEN RESEARCH FOUNDATION VZW

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 8 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
28.12.2004	17.05.2005

Name and mailing address of the international preliminary examining authority:

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/001209

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-34 as originally filed

   Sequence listings part of the description, Pages

   35-38 as originally filed

   Claims, Numbers

   1-13 as originally filed

   Drawings, Sheets

   1/8-8/8 as originally filed

   ☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-9,11-13 (all partially)

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1-9,11-13 (all partially) (see separate sheet)

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-13
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-13
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-13
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Supplemental Box relating to Sequence Listing

Continuation of Box I, item 2:

1. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this report has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☒ contained in the international application as filed

   ☒ filed together with the international application in computer readable form

   ☐ furnished subsequently to this Authority for the purposes of search and/or examination

   ☐ received by this Authority as an amendment on

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional observations, if necessary:

Re Item III.

Claims 1-9,11-13 relate to a compound defined by reference to a desirable characteristic or property, namely " inhibitor of PACAP signalling.....", "inhibitor inhibits...", " inhibitor is selected from the group consisting of ...a small molecule, a ribozyme, ...and a tetrameric peptide", "cyclic lactam analogues of PACAP", " PACAP receptor blocking cyclic lactam PACAP analogues", "N-terminal truncated or substituted VIP peptide PACAP receptor blockers", or "..an additional compound for enhancing megakaryocyte maturation". The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to PACAP inhibitors as clearly specified in claim 9 ,10, and the description (page 3, line 25-30), the additional compounds for enhancing megakaryocyte maturation as specified in claim 13, for the treatment of thrombocytopenia; and with due respect to the general idea of the invention.

No opinion will be given in respect of subject matter which is not covered by the search report (Rule 66.1(e)PCT)

Re Item V.

The following documents are referred to in this communication:

D1 : US5486472
D3: XP008036813

1 NOVELTY (Article 33(2) PCT)

1.1 The subject matter of the present application, insofar as clear, is new over

the prior art. The use of an inhibitor of PACAP signalling, as clearly specified in claims 9,10 and the description of the present application, for the therapy of thrombocytopenia was not disclosed. In addition, a pharmaceutical composition comprising an inhibitor PACAP signalling and thrombopoetin or Interleukin 11 (compound for enhancing magakaryocyte maturation) was not disclosed.

Therefore the present application meets the criteria of Article 33(1) PCT, because the subject-matter of claims 1-13 is new in the sense of Article 33(2) PCT.

2 INVENTIVE STEP (Article 33(3) PCT)

2.1 The use of inhibitors of PACAP signalling for the therapy of PACAP related diseases was known (see Document D1, which discloses a monoclonal antibody specific for PACAP 1-38, PACAP 1-27 for development of assays or for diagnosis and treatment of diseases related to PACAP (cf. column 1, line 5-10). However, no mention is made of any such diseases, particularly the use of inhibitors of PACAP signalling for the prevention or treatment of thrombocytopenia is not indicated. Document D3 discloses inhibition of platelet activation by VIP (thus describes an effect of another member of the VIP-glucagon-growth hormone releasing factor-secretin superfamily on the activity of platelets). However, based on the inhibitory effect of VIP on platelet activity, a stimulation of platelet activation by inhibitors of the PACAP-signalling cannot be deduced. In particular D3 does not disclose the use of VIP for the treatment of thrombocytopenia.

Thus the prior art thus does not suggest the use of an inhibitor of PACAP signalling for the prevention or treatment of thrombocytopenia (the sole effect of platelet activation would not be considered of therapeutic interest in the context of thrombocytopenia (severe shortage of the number of platelets)).

Therefore the subject matter of claims 1-13, insofar as clear, is inventive according to Article 33(3) PCT.

3 INDUSTRIAL APPLICABILITY (Article 33(4) PCT)

Claims 1-13, insofar as clear, fulfil the requirements of (Article 33(4) PCT).

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (SEPARATE SHEET)

International application No.

PCT/EP2004/001209